ACUTE TOXICITY SUMMARY

VANADIUM PENTOXIDE

(divanadium pentoxide, vanadic anhydride, vanadium oxide)

CAS Registry Number: 1314-62-1

I. Acute Toxicity Summary (for a 1-hour exposure)

Inhalation reference exposure level	**30 μg/m³**
Critical effect(s)	coughing, increased mucus production in healthy human volunteers
Hazard Index target(s)	Respiratory System; Eyes

II. Physical and Chemical Properties (HSDB, 1994 except as noted)

Description	yellow to rust-brown solid (ACGIH, 1986)
Molecular formula	V_2O_5
Molecular weight	181.88 g/mol
Density	3.357 g/cm^3 @ 18°C
Boiling point	1750°C
Melting point	690°C
Vapor pressure	not applicable
Flashpoint	not applicable
Explosive limits	not applicable
Solubility	soluble in acetone, concentrated acid and alkali; slightly soluble in water; insoluble in alcohol
Odor threshold	not applicable
Metabolites	none reported (Friberg *et al.*, 1986)
Conversion factor	not applicable

III. Major Uses or Sources

Vanadium pentoxide (V_2O_5) is used as a catalyst in oxidation reactions in the production of sulfuric acid and plastics (Friberg *et al*., 1986). It is also used as a mordant in dyeing, and as a component of photographic developer (Sax, 1984). In the manufacture of glass, it is used as a depolarizer and inhibitor of UV light. V_2O_5 is also released by the combustion of fossil fuels which contain small amounts of vanadium (NAS, 1974).

IV. Acute Toxicity to Humans

Inhalation of V_2O_5 fumes, released during the production of V_2O_5 and during boiler cleaning, may result in irritation of the eyes and respiratory tract and in bronchospasm (Friberg *et al*., 1986). The onset of symptoms occurs 1-6 days after exposure. Subsequent exposures to V_2O_5

may result in increased severity of symptoms, most likely a result of sensitization (Zenz *et al.*, 1962). The eye irritation threshold is reported to be 0.5 mg/m³ (Reprotext, 1994). The respiratory irritation threshold is reported to be below that of ocular irritation (Grant, 1986).

High level acute exposures may result in CNS effects including paralysis, respiratory depression, convulsions, and death (Reprotext, 1994).

Zenz and Berg (1967) studied human sensory responses to controlled vanadium pentoxide exposures in 9 male volunteers. The men were exposed for one 8 hour period to 1.0, 0.25 or 0.1 mg/m^3 of V_2O_5. The 2 volunteers exposed to 1.0 mg/m^3 began to cough during the latter half of the exposure. The coughing persisted for 8 days after exposure. Five subjects were exposed to 0.25 mg/m^3. On the morning following their exposure, all five unexpectedly developed a loose, productive cough which lasted 7 to 10 days. The 2 volunteers exposed to 0.1 mg/m^3 V_2O_5 showed no symptoms during or immediately after exposure but within 24 hours they formed considerable mucus which subsided after 4 days.
Workers exposed to 0.1-0.3 mg/m³ V_2O_5 for a minimum of 6 months reported symptoms of eye, nose, and throat irritation and exhibited signs of pharyngeal infection, green tongue and wheezing or rales (Lewis, 1959).

Predisposing Conditions for Vanadium Pentoxide Toxicity

Medical: Persons with preexisting skin, eye, kidney, or respiratory conditions, especially chronic bronchitis or asthma, or other underlying cardiopulmonary disease may be more sensitive to the toxic effects of V_2O_5 (Reprotext, 1999).

Chemical: Persons exposed simultaneously to phthalic anhydride and V_2O_5 may be at greater risk for exacerbation of asthma. Persons exposed to other vanadium compounds may be more sensitive to the effects of V_2O_5 exposure (Reprotext, 1999).

V. Acute Toxicity to Laboratory Animals

Exposure to V_2O_5 at a concentration of 500 mg/m³ for 23 minutes was found to be lethal in cats (Heimberger, 1929). Gastroenteritis, pneumonitis, and pulmonary edema were observed at autopsy. An LC_{LO} of 205 mg/m³ V_2O_5 for a 7-hour exposure was reported for rabbits (Sjoberg, 1950). Autopsy results revealed marked tracheitis, bronchopneumonia, and pulmonary edema. In this same study, rabbits exposed to 20-40 mg/m³ V_2O_5 for 1 hour per day for "several months" (exact duration not specified) exhibited chronic rhinitis and tracheitis, emphysema and patches of lung atelectasis with bronchopneumonia.

Sixteen adult, male cynomolgus monkeys were acutely exposed by whole-body inhalation of V_2O_5 dust (0.5 mg or 5.0 mg/m³) at 1 week intervals (Knecht *et al.*, 1985). Pulmonary function tests were performed one day after each inhalation exposure, and inflammation was studied by cytologic analysis of lower respiratory tract cells by bronchoalveolar lavage (BAL). Pre-exposure comparisons were used in place of controls. Reduction in air-flow in central and peripheral airways was noted without any change in parenchymal function. V_2O_5 dust exposures led to a

significant increase in the total cell counts recovered from the lungs by BAL, including very large increases in absolute number and relative percentage of polymorphonuclear leukocytes (PMN).

Rats (200-250 g) were intratracheally administered vanadium compounds or vehicle (as a control) (Pierce *et al*., 1996). The soluble vanadium compounds $NaVO_3$ and $VOSO_4$ induced rapid and intense pulmonary inflammation and inflammatory cytokine mRNA expression while the less soluble V_2O_5 was much less potent. Significant neutrophil influx was noted 24 hours after V_2O_5 exposure and persisted for several days. Analysis of lavage fluid, BAL cells, and lung suggested rapid clearance of the V_2O_5 from the lung surface and accumulation in BAL cells and lung tissue.

VI. Reproductive or Developmental Toxicity

No studies of reproductive toxicity in humans were available (Reprotext, 1994).

Pregnant mice injected with a total dose of 28 µg V_2O_5 (delivered as 0.15 ml of a 1.0 mM V_2O_5 solution) on the eighth day of gestation exhibited a significant increase in number of fetuses with delayed skeletal ossification as compared to controls (Wide, 1984). Additionally, six of the exposed fetuses had "broken spinal cords".

Pregnant Wistar rats were administered V_2O_5 by intraperitoneal injections on days 6-15 (3 mg/kg/day) or 9-12 (5 mg/kg/day) of gestation (Zhang *et al*., 1993a). Single doses (5 mg/kg/day) were also given on days 9, 10, or 11. Decreased maternal weight gain was noted. Effects observed included decreased weight gain, increased fetal mortality, decreased fetal weight, delayed bone ossification, subcutaneous hemorrhage, and dilation of lateral ventricles and renal pelvis. The greatest effects were noted from exposures on day 10. In a second study, pregnant Wistar rats were administered 0.33, 1, or 3 mg/kg-day over days 6-15 of gestation (Zhang *et al.*, 1993b). Adverse effects similar to that reported in the companion paper (Zhang *et al*., 1993a) were noted in the two higher dose groups but not in the low dose group.

Effects of vanadium pentoxide treatment on male mouse reproductive function were investigated (Altamirano-Lozano *et al*., 1996). Sperm count, motility, and morphology were adversely affected, and decreased fertility rate was reported after intraperitoneal injection of 8.5 mg V_2O_5 per kg body weight.

VII. Derivation of Acute Reference Exposure Level and Other Severity Levels (for a 1-hour exposure)

Reference Exposure Level (protective against mild adverse effects): 30 µg/m³

Study	Zenz and Berg, 1967
Study population	nine healthy human volunteers
Exposure method	8 hour exposures to 0.1, 0.25 or 1.0 mg/m³ V_2O_5
Critical effects	subjective reports of increased respiratory mucus production that was cleared by coughing.

LOAEL	0.25 mg/m³ V_2O_5 (n = 5) 0.1 mg/m³ V_2O_5 (n = 2)	*NOAEL/LOEL*
Exposure duration	8 hours	
Equivalent 1 hour concentration	0.3 mg/m³ (C^2 * 1 hr = [0.1 mg/m³]^2 * 8 hrs)	
LOAEL uncertainty factor	1 (effect observed was not adverse)	
Interspecies uncertainty factor	1	
Intraspecies uncertainty factor	10	
Cumulative uncertainty factor	10	
Reference Exposure Level	0.03 mg/m³ (30 µg/m³)	

Level Protective Against Severe Adverse Effects

No recommendation is made due to the limitations of the database.

Level Protective Against Life-threatening Effects

No recommendation is made due to the limitations of the database.

A NIOSH-IDLH of 35 mg/m³ has been presented, but the method for deriving this value was not reported (NIOSH, 1995).

VIII. References

Altamirano-Lozano M, Alvarez-Barrera L, Basurto-Alcantara F, Valverde M, Rojas E. Reprotoxic and genotoxic studies of vanadium pentoxide in male mice. Teratog Carcinog Mutagen 1996;16(1):7-17.

American Conference of Governmental Industrial Hygienists (ACGIH). Documentation of the Threshold Limit Values and Biological Exposure Indices. 5th ed. Cincinnati (OH): ACGIH; 1986. p. 620.

Friberg L, Norberg GF, Vouk VB, editors. Handbook of the toxicology of metals. Vol II: Specific metals. 2nd ed. Amsterdam: Elsevier; 1986. p. 638-663.

Grant WM. Toxicology of the eye. Springfield (IL): CC Thomas; 1986. p. 970.

Hazardous Substances Data Bank (HSDB). National Library of Medicine, Bethesda (MD) (CD-ROM version). Denver (CO): Micromedex, Inc.; 1994.

Heimberger C. Injektionsversuche an Katzen und Mausen mit Vanadinsalzlosungen und Staubinhalationsversuche and Katzen mit Vanasiumpentoxyd. Inaug Diss, Becker, Wurzburg, 1929 [cited in Hudson, 1964].

Hudson TGF. Vanadium: toxicology and biological significance. In: Browning E, editor. Elsevier monographs on toxic agents. Amsterdam: Elsevier; 1964. p. 67-78.

Knecht EA, Moorman WJ, Clark JC, Lynch DW, Lewis TR. Pulmonary effects of acute vanadium pentoxide inhalation in monkeys. Am Rev Respir Dis 1985;132(6):1181-1185.

Lewis CE. The biological effects of vanadium. II. The signs and symptoms of occupational vanadium exposure. AMA Arch Indust Health 1959;19(5):497-503.

National Academy of Sciences (NAS). Medical and biologic effects of environmental pollutants: Vanadium. Committee on biologic effects of atmospheric pollutants, Division of Medical Sciences, National Research Council. Washington (DC): NAS; 1974. p. 5.

NIOSH. Vanadium dust. Chemical listing and documentation of revised IDLH values (as of March 1, 1995). Available at http://www.cdc.gov/niosh/intridl4.html.

Pierce LM, Alessandrini F, Godleski JJ, Paulauskis JD. Vanadium-induced chemokine mRNA expression and pulmonary inflammation. Toxicol Appl Pharmacol 1996;138(1):1-11.

Reprotext® System. Dabney BJ, editor. Denver (CO): Micromedex, Inc.; 1994. (Edition expires 1/31/1994).

Reprotext® System. Dabney BJ, editor. Denver (CO): Micromedex, Inc.; 1999. (Edition expires 1/31/1999).

Sax NI. Dangerous properties of hazardous materials. 6th ed. New York: Van Nostrand Reinhold; 1984. p. 2718.

Sjoberg SG. Vanadium pentoxide dust. A clinical and experimental investigation of its effects after inhalation. Acta Med Scand 1950;(238 Suppl):138:1 [cited in Hudson, 1964].

Wide M. Effect of short-term exposure to five industrial metals in the embryonic and fetal development of the mouse. Environ Res 1984;33:47-53.

Zenz C, Bartlett JP, Thiede WH. Acute vanadium pentoxide intoxication. Arch Environ Health 1962;5:542-546.

Zenz C, Berg BA. Human responses to controlled vanadium pentoxide exposure. Arch Environ Health 1967;14:709-712 [cited in NAS, 1974].

Zhang T, Gou X, Yang Z. [Study of teratogenicity and sensitive period of vanadium pentoxide in Wistar rats]. Hua Hsi I Ko Ta Hsueh Hsueh Pao 1993a;24(2):202-205 [Article in Chinese, English abstract reviewed].

Zhang T, Yang Z, Zeng C, Gou X. [A study on developmental toxicity of vanadium pentoxide in Wistar rats]. Hua Hsi I Ko Ta Hsueh Hsueh Pao 1993b;24(1):92-96 [Article in Chinese, English abstract reviewed].